

**What is claimed is:**

1. A method for determining whether a test subject has at least one auto-immune disease comprising
  - a) obtaining blood from the predetermined test subject thus obtaining a test sample;
  - b) obtaining blood from a non-autoimmune subject thus obtaining a control sample;
  - c) contacting the test sample and the control sample with a combination of at least one detectably-labeled anti-CD4 antibody and at least one detectably-labeled anti-CD40 antibody;
  - d) detecting the level of CD4<sup>lo</sup>CD40<sup>hi</sup> T cells in the test sample and in the control sample;  
wherein when there is an increase in the level of CD4<sup>lo</sup>CD40<sup>hi</sup> T cells in the test sample as compared to the level of CD4<sup>lo</sup>CD40<sup>hi</sup> T cells in the control sample, the test subject has at least one auto-immune disease.
2. The method of claim 1 further comprising isolating the test sample CD4<sup>lo</sup>CD40<sup>hi</sup> T cells and the control sample CD4<sup>lo</sup>CD40<sup>hi</sup> T cells from part 1d) and determining the presence or absence of an increase in production of at least one cytokine in the test T cell population as compared to the sample T cell population.
3. The method of claim 2 wherein said cytokine is at least one cytokine selected from the group consisting of IL-2, IL-4, IL-6, IL-10, TGF $\beta$  and IFN $\gamma$ .
4. The method of claim 1, wherein the auto-immune disease is selected from the group consisting of type 1 diabetes, rheumatoid arthritis, lupus, multiple sclerosis, atherosclerosis, Crohn's colitis, ulcerative gastritis, primary biliary cirrhosis, chronic obstructive pulmonary disease (COPD) and scleroderma.
5. The method of claim 4, wherein the auto-immune disease is type 1 diabetes.
6. The method of claim 4, wherein the COPD disease is emphysema.

7. The method of claim 1, wherein said detecting is by flowcytometry.

8. The method of claim 1, wherein said subject is human.

9. A method for determining whether a predetermined test subject is susceptible to developing at least one predetermined auto-immune disease comprising

a) obtaining a first sample of blood from said predetermined test subject;

b) obtaining a second sample of blood from said same subject;

c) detecting the CD4<sup>lo</sup> CD40<sup>hi</sup> T cell population in said first and second samples;

d) contacting said second test sample with at least one predetermined antigen indicative of at least one predetermined auto-immune disease for a length of time and in an amount sufficient to obtain a positive or negative cellular response in the CD4<sup>lo</sup> CD40<sup>hi</sup> T cell population of said second sample,

e) determining whether a positive or negative cellular response occurs in the CD4<sup>lo</sup> CD40<sup>hi</sup> T cell population of said first and said second samples by measuring at least one response selected from the group consisting of CD4<sup>lo</sup> CD40<sup>hi</sup> T cell proliferation, CD4<sup>lo</sup> CD40<sup>hi</sup> T cell death and CD4<sup>lo</sup> CD40<sup>hi</sup> cytokine production,

wherein when a positive response occurs in the CD4<sup>lo</sup> CD40<sup>hi</sup> T cell population of the second sample as compared to the response from the CD4<sup>lo</sup> CD40<sup>hi</sup> T cell population of the first sample, the predetermined subject is susceptible to developing the at least one predetermined autoimmune disease.

10. The method of claim 9, wherein a positive response is an increase in CD4<sup>lo</sup> CD40<sup>hi</sup> T cell proliferation, an increase in CD4<sup>lo</sup> CD40<sup>hi</sup> T cell death and an increase in production of at least one cytokine produced by said CD4<sup>lo</sup> CD40<sup>hi</sup> T cell population.

11. The method of claim 10 wherein said at least one cytokine is selected from the group consisting of IL-2, IL-4, IL-6, IL-10, TGF $\beta$  and IFN $\gamma$ .

12. The method of claim 9 wherein said at least one preselected auto-immune disease is type 1 diabetes and said antigen is pancreatic tissue.

13. The method of claim 9 wherein said at least one preselected auto-immune disease is rheumatoid arthritis and said antigen is synovial tissue.

14. The method of claim 9, wherein said at least one preselected auto-immune disease is multiple sclerosis and said antigen is nervous tissue.

15. The method of claim 9, wherein said at least one preselected auto-immune disease is scleroderma and said antigen is skin tissue.

16. The method of claim 9, wherein said at least one auto-immune disease is atherosclerosis and said antigen is cardiac tissue.

17. The method of claim 9, wherein said subject is human.

18. A method of modulating the proliferation of CD4<sup>lo</sup> CD40<sup>hi</sup> T cells in a subject in need of said modulation comprising at least one method selected from the group consisting of

- a) contacting said subject with at least one agent which inhibits the activation of RAG recombinase activity;
- b) contacting said subject with an antibody molecule, or fragment thereof, to CD40;
- c) contacting said subject with an antibody molecule, or fragment thereof, to CD154;
- d) contacting said subject with at least one blocking peptide to prevent interaction of the CD40 receptor with the CD154 ligand;
- e) contacting said subject with at least one RNA molecule specifically hybridizing to the RAG2 gene product; and,
- f) contacting said subject with at least one RNA molecule specifically hybridizing to the RAG1 gene product;

wherein said contacting is for a length of time sufficient and in an amount sufficient to modulate the proliferation of CD4<sup>lo</sup> CD40<sup>hi</sup> T cells in said subject.

19. The method of claim 18, part a), wherein said at least one agent is a chaetochromin or a derivative thereof.

20. The method of claim 18, part b), wherein said antibody fragment is an Fab portion.
21. The method of claim 18, part c), wherein said antibody fragment is an Fab portion.
22. The method of claim 18, part d), wherein said blocking peptide is selected from the group consisting of SSKTTSVLQWAEKGYYTMSNNLVT (SEQ ID NO: 7) and QIAAHVISEASSK (SEQ ID NO: 8).
23. The method of claim 18, part e), wherein said RNA molecule is selected from the group consisting of  
5'-AUGUCUCUGCAGAUGGUACdAdG-3' (SEQ ID NO: 9);  
5'-CUGUUACCAUCUGCAGAGACdAdU-3' (SEQ ID NO: 10);  
5'-GGUAGGAGAACUUCCUGAAGdCdC-3' (SEQ ID NO: 11);  
5'-GGGAUGGGCACUGGGUCCAUGdCdU-3' (SEQ ID NO: 12);  
5'-AGCAUGGACCCAGUGGCCAUCCdCdC-3' (SEQ ID NO: 13); and,  
5'-CUGUUACCAUCUGCAGAGACdAdU-3' (SEQ ID NO: 14).
24. The method of claim 18, part f), wherein said RNA molecule is selected from the group consisting of  
5'-AUGGCAGCCUCUUUCCACCCAdCdC-3' (SEQ ID NO: 15);  
5'-GGUGGGUGGGAAAGAGGGCUGCCdAdU-3' (SEQ ID NO: 16);  
5'-AAACUUGCAGCUCAGCAAAAAACdTdC-3' (SEQ ID NO: 17);  
5'-GAGUUUUUUGCUGAGCUGCAAGUdUdU-3' (SEQ ID NO: 18);  
5'-GAGUUUUUUGCUGAGCUGCAAGUdUdU-3' (SEQ ID NO: 19);  
5'-UCACAAAACCCUGGCCAUGUdCdC-3' (SEQ ID NO: 20); and,  
5'-GGAACAUGGGCCAGGGUUUUGUdGdA-3' (SEQ ID NO: 21).
25. The method of claim 18, wherein said subject has an increased level of CD4<sup>lo</sup>CD40<sup>hi</sup> T cells as compared to the level of CD4<sup>lo</sup>CD40<sup>hi</sup> T cells in a non-auto-immune subject and the modulation is a decrease in the level of CD4<sup>lo</sup>CD40<sup>hi</sup> T cells.

26. The method of claim 18, wherein said subject is human.
27. A kit for detecting CD4<sup>lo</sup>CD40<sup>hi</sup> T cells comprising
  - a) at least one detectably labeled anti-CD4 antibody and at least one detectably labeled anti-CD40 antibody; and,
  - b) at least one predetermined antigen indicative of at least one predetermined autoimmune disease.